

---

**Deletion of Pten expands lung epithelial progenitor pools and confers resistance to airway injury.**

**Journal:** Am J Respir Crit Care Med

**Publication Year:** 2009

**Authors:** Caterina Tiozzo, Stijn De Langhe, Mingke Yu, Vedang A Londhe, Gianni Carraro, Min Li, Changgong Li, Yiming Xing, Stewart Anderson, Zea Borok, Saverio Bellusci, Parviz Minoo

**PubMed link:** 19574443

**Funding Grants:** CIRM Stem Cell Biology Training Grant

**Public Summary:**

**Scientific Abstract:**

**RATIONALE:** Pten is a tumor-suppressor gene involved in stem cell homeostasis and tumorigenesis. In mouse, Pten expression is ubiquitous and begins as early as 7 days of gestation. Pten(-/-) mouse embryos die early during gestation indicating a critical role for Pten in embryonic development. **OBJECTIVES:** To test the role of Pten in lung development and injury. **Methods:** We conditionally deleted Pten throughout the lung epithelium by crossing Pten(flox/flox) with Nkx2.1-cre driver mice. The resulting Pten(Nkx2.1-cre) mutants were analyzed for lung defects and response to injury. **MEASUREMENTS AND MAIN RESULTS:** Pten(Nkx2.1-cre) embryonic lungs showed airway epithelial hyperplasia with no branching abnormalities. In adult mice, Pten(Nkx2.1-cre) lungs exhibit increased progenitor cell pools composed of basal cells in the trachea, CGRP/CC10 double-positive neuroendocrine cells in the bronchi, and CC10/SPC double-positive cells at the bronchioalveolar duct junctions. Pten deletion affected differentiation of various lung epithelial cell lineages, with a decreased number of terminally differentiated cells. Over time, Pten(Nkx2.1-cre) epithelial cells residing in the bronchioalveolar duct junctions underwent proliferation and formed uniform masses, supporting the concept that the cells residing in this distal niche may also be the source of procarcinogenic stem cells. Finally, increased progenitor cells in all the lung compartments conferred an overall selective advantage to naphthalene injury compared with wild-type control mice. **CONCLUSIONS:** Pten has a pivotal role in lung stem cell homeostasis, cell differentiation, and consequently resistance to lung injury.

---

**Source URL:** <http://www.cirm.ca.gov/about-cirm/publications/deletion-pten-expands-lung-epithelial-progenitor-pools-and-confers>